DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

WARNING LETTER
VIA EXPRESS

AUG * 3 2000

Mr. Volker Brinke
General Manager
Almo Erzeugnisse Erwin Busch GmbH
GroBe Allee 84
34454 Bad Arolsen, Germany

Dear Mr. Brinke:

During an inspection of your firm located in Bad Arolsen, Germany, on May 8-11, 2000 our investigator determined that your firm manufactures disposable syringes. These products are devices as defined by Section 201(h) of the Federal, Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Quality System Regulation, as specified in Title 21, Code of Federal Regulation (CFR), Part 820, as follows:

1. Failure to validate with a high degree of assurance a process that cannot be fully verified by subsequent inspection and test, as required by 21 CFR 820.75(a). For example:

   a. No validation was performed for the ethylene oxide sterilization aeration room.

   b. No validation was performed to ensure that your device production rooms met the US Federal Standard 209E, 100,00 Clean Room Classification for PIC Class D standard, as required by your B.Braun SOP, Document Number 75139-11, dated 12/15/98.

2. Failure to adequately establish procedures for implementing corrective and preventive action, as required by 21 CFR 820.100(a). For example:

   a. Your CAPA procedures for project Beschadigte Kolben, dated 01/21/00, were not being followed with respect to the discontinued use of transport carts without protective side walls. On 5/10/00, the investigator observed 16 device component transport carts without the protective walls containing device components in the production assembly area.

   b. There is no documentation that your Quality System procedure, QM-Handbuch Grundsatzerklarung zur Qualitatspolitik, dated 9/3/99, was followed for the approval and implementation of CAPA Project, Beschadigte Kolben, dated 01/21/00, in that:

- There is no documentation that Technik and Quality Control approved the implementation of this CAPA project, as required by your SOP Wochenbesprechung Technik/Qualitat, procedure number QW-VA 14.18.0100, dated 02/04/00.
- There is no documentation that Quality Assurance approved the implementation of this CAPA project, as required by your SOP.
- There is no documentation that the Quality System Review Board was notified of the approval and implementation of this CAPA project, as required by your SOP Review der obersten Leitung, procedure number QW-VA 01.21.0000, dated 01/05/00.

3. Failure to establish and maintain procedures to adequately control environmental conditions when these conditions could reasonably be expected to have an adverse effect on product quality, as required by 21 CFR 820.70(c). For example:

   a. Two of three large screened windows that were opened to the outside facility wall of the building were allowing outside environmental conditions inside of the equipment maintenance room.
   b. Two metal grinding tool/art making machines were located in your equipment maintenance room, and located on the floor around the machines and throughout the room were large amounts of metal fragments on the wheels of machine tool carts and transport carts, and on the shoe soles of the maintenance room manager.
   c. Maintenance employees routinely enter and exit the equipment maintenance room through the device assembly room entrance door to perform maintenance activities in the device production area.

4. Failure to adequately maintain procedures to ensure that the design requirements relating to a device are appropriate and address the intended use of the device, including the needs of the user and patient, as required by 21 CFR 820.30(c). For example:

   a. There is no raw data test results for qualification test plan P10-5-002 and P10-5-001.

   b. There is no documentation that the test method requirements (Method 0103) for temperature, humidity, and room lighting were met to perform this test prior to completion of test plan report P10-5-002.

In addition to the above observations, we have concerns regarding your sterilization process validation. It appears that you performed 3 half cycles during validation, but no full cycle. If this is the case, how do you know what effects a full cycle could have on the device? How was the bioburden of the device determined? How did you demonstrate that the sterilization process is effective in destroying the bioburden? How do you control particulates, more specifically, the metal grindings observed by the investigator in the manufacturing areas, from effecting the device? Lastly, we request that you submit your sterilization validation protocol and results.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the form FDA 483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance system. You are responsible for investigating and determining the causes of the violations identified by the Food and Drug Administration. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

We acknowledge receipt of your June 30, 2000, response to the FDA 483. However, our review indicates that it is inadequate in that you have not carried out your corrective actions, but plan to do so by January 2001.

Please notify this office in writing within 15 days of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make correction to any underlying systems problems necessary to assure that similar violations will not recur. Please include any and all documentation to show that adequate correction has been achieved. In the case of future corrections, an estimated date of completion, and documentation showing plans for correction, should be included with your response to this letter.

If documentation is not in English, please provide an English translation to facilitate our review. Please address your response and any questions to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement II, General Hospital Devices Branch, HFZ-333, 2098 Gaither Road, Rockville, Maryland 20850, to the attention of Ms. Carolyn Niebauer.

Should you require any assistance in understanding the contents of this letter, do not hesitate to contact Ms. Leslie E. Dorsey at the letterhead address or at 301.594.4618 or FAX 301.594.4638.

Sincerely yours,

Steven M. Niedelman
Acting Director
Office of Compliance
Center for Devices and Radiological Health